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14. ABSTRACT During this seventh year of the project, we were open for enrollment at the University of Pittsburgh until January, 2015, when the cardiac surgeon involved in the project left the University. We therefore suspended enrollment until he can be replaced. During the time the study was open, no appropriate candidates were identified. The investigators discussed ways to expand the eligibility criteria for the study. It was felt that patients who arrive at the hospital with a pulse, but then develop cardiac arrest in the operating room, rather than in the emergency department, represent an appropriate patient population to be included. The Data and Safety Monitoring Board, as well as the Food and Drug Administration, have agreed to this change in the protocol. At the University of Maryland, the IRB asked the study team to submit the proposal as a new project because of changes to the protocol and Dr. Tisherman's conflict of interest. The conflict of interest was vetted with the University's Conflict of Interest Officer. The plan for management of the conflict used at the University of Pittsburgh was adopted. The IRB has approved the community consultation, public disclosure process. Community consultation and training for the trauma surgeons involved in the project are scheduled to begin in October. To better understand the patient population for this study, we have initiated a retrospective study of trauma patients who suffered a cardiac arrest and underwent a thoracotomy in the Trauma Resuscitation Unit of the Shock Trauma Center.

15. SUBJECT TERMS
Trauma, hemorrhagic shock, cardiac arrest, cardiopulmonary resuscitation, hypothermia

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Introduction

Cardiopulmonary resuscitation (CPR) can save victims of normovolemic cardiac arrest (CA), e.g., ventricular fibrillation. During exsanguination CA from trauma, however, CPR, even with an emergency department (ED) thoracotomy and open chest CPR, results in unacceptably low survival rates. *Emergency Preservation and Resuscitation (EPR)* was developed to rapidly preserve the organism during ischemia, using hypothermia, drugs, and fluids, to "buy time" for transport and resuscitative surgery. The purpose of this study is to test the feasibility of rapidly inducing profound hypothermia ($\leq 10^{o}C$) with an aortic flush in trauma victims that have suffered CA and failed standard resuscitative efforts to enable resuscitative surgery and delayed resuscitation with cardiopulmonary bypass. The primary outcome variable will be survival to hospital discharge with minimal neurologic dysfunction.

Body

Scientific Progress

In December, 2009, we conducted the first meeting of the Data and Safety Monitoring Board. The group approved moving forward with the study. They recommended standardization of the transfusion protocols across sites, elimination of blunt trauma victims, and the use of Seldinger technique for aortic cannulation. In subsequent meetings, they have also asked for more prolonged follow-up of subjects (to 12 months), including additional functional outcome using the SF-36 form. They further recommended that the trauma surgeons involved in the study obtain hospital privileges for cannulation for the EPR flush. This has been accomplished.

Given the complexity of our planned intervention for trauma patients in cardiac arrest, we need to optimize subject inclusion and exclusion criteria. The literature on such patients is scant, with studies focusing on mortality rates and crude information such as signs of life (pulse, breathing, spontaneous movements) in the field or emergency department and admission cardiac rhythm. To better define this patient population to optimize subject selection, we have initiated a retrospective study to look at other factors that could be quickly determined during the resuscitation of a trauma patient in the emergency department. This retrospective study should produce publishable data, although so far we have not obtained sufficient data from the University of Pittsburgh to make any conclusions. We have initiated a similar study at the University of Maryland.

Separately, to better profile patients who die from trauma, Dr. Tisherman led a study of the hemorrhagic shock database of the Resuscitation Outcomes Consortium, which studies prehospital care in patients with life-threatening injuries. Within this database, we have identified 67 patients with hemorrhagic shock and no significant head injury who died within 24 hours of their injuries. These patients represented 83% of all deaths in the shock cohort. The primary cause of these early deaths was indeed hemorrhage. Twenty-six patients died in the Emergency Department. Data on timing of pulselessness and use of ED thoracotomies is not available in the database. Presumably, many of these patients could have been EPR candidates. Overall, this dataset suggests that the great majority of deaths from traumatic hemorrhage occur within 24 hrs from direct effects of hemorrhage. Late deaths are rare. To improve survival from traumatic hemorrhagic shock, early, novel interventions, such as EPR, are needed.

Administrative and Logistic Matters

The first regulatory step for proceeding with this study was to obtain an Investigational Device Exemption (IDE) from the Food and Drug Administration (FDA). Our trial is complicated by the fact that both fluids and equipment are to be used for an application that is not currently approved by the FDA. We have now obtained an investigator-sponsored IDE from the FDA Center for Devices and Radiological Health Office of Device Evaluation.

With the approval of the IDE, we were able to obtain approval for the proposal from the University of Pittsburgh Institutional Review Board (IRB) as both the coordinating center and participating site. We have now completed the community consultation and public disclosure processes. These included the meetings with the Pittsburgh Human Relations Commission and the University of Pittsburgh Center for Minority Health, a random-digit telephone survey, surveys in trauma clinic, town hall meetings at the University Student Union, a website, and publicity in local and national media. The results were presented to the IRB and IRB approval has been granted. We have also obtained human use approval from the USAMRMC.

Similarly, the University of Maryland IRB has preliminarily approved the study pending completion of the community consultation process. Other centers that have been identified for

possible inclusion in the study in the future include the Oregon Health and Sciences University, the University of Pennsylvania, the University of Texas – Houston, and the University of Colorado. Until both the University of Pittsburgh and the University of Maryland are actively enrolling, we will not consider initiating these sites.

Because Drs. Tisherman and Kochanek are co-authors of a submitted patent for EPR Methods, the Universities of Pittsburgh and Maryland Conflict of Interest Offices have reviewed the plans for the trial and defined a plan to resolve the conflict so that these researchers could still be involved in the study.

Key Research Accomplishments

During this past year, we have achieved 2 important goals. 1) We have revised the enrollment criteria to include patients who arrive at the hospital with a pulse and then suffer a cardiac arrest in the operating room, rather than the emergency department. 2) We received approval of the community consultation plan at the University of Maryland and have scheduled the initial events.

We have continued to work on gathering the necessary historical data for the study. This study was approved at the University of Maryland and data has been obtained from the trauma registry. We have initiated chart reviews for patients with penetrating trauma who underwent a thoracotomy in the Trauma Resuscitation Unit in the past 5 years.

Reportable Outcomes

We have not enrolled any patients in the study.

Conclusion

Most of the work so far on this project has been focused on the regulatory and training processes. We have an IDE and full approval from 1 IRB, plus approval pending community consultation from another. We had been ready for enrollment at the University of Pittsburgh. We are making progress with readiness at the University of Maryland.

References

None